Fig. 1/3

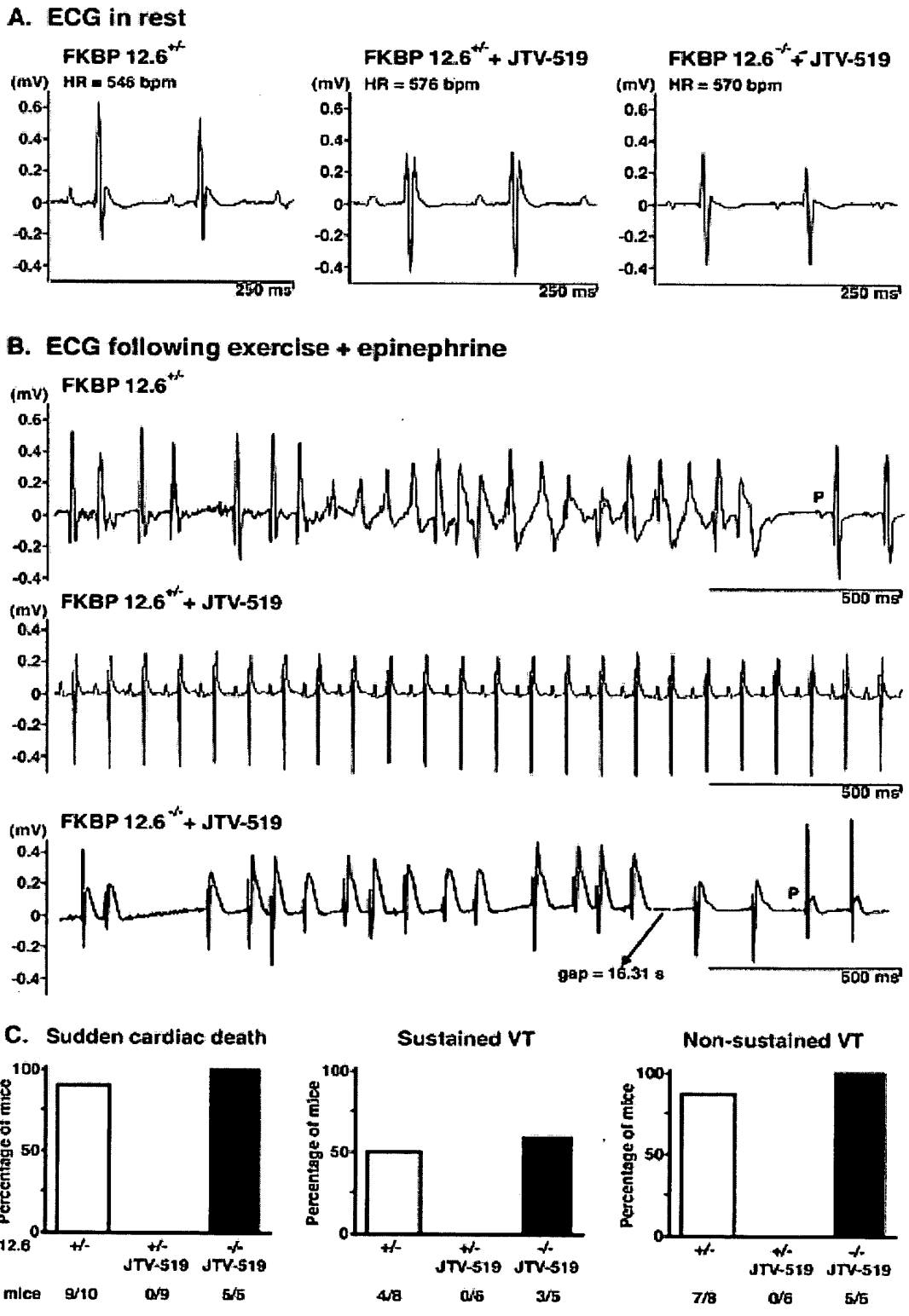

A. ECG in rest
FKBP 12.6+/-
(mV) HR = 546 bpm
FKBP 12.6+/- + JTV-519
(mV) HR = 576 bpm
FKBP 12.6-/- + JTV-519
(mV) HR = 570 bpm
0.6
0.4
0.2
0
-0.2
-0.4
250 ms
B. ECG following exercise + epinephrine
FKBP 12.6+/-
FKBP 12.6+/- + JTV-519
FKBP 12.6-/- + JTV-519
(mV)
P
500 ms
gap = 16.31 s
C. Sudden cardiac death
Sustained VT
Non-sustained VT
Percentage of mice
100
50
0
FKBP12.6
+/-
+/- JTV-519
-/- JTV-519
No. of mice
9/10
0/9
5/5
4/8
0/6
3/5
7/8
0/6
5/5

Fig. 2/3

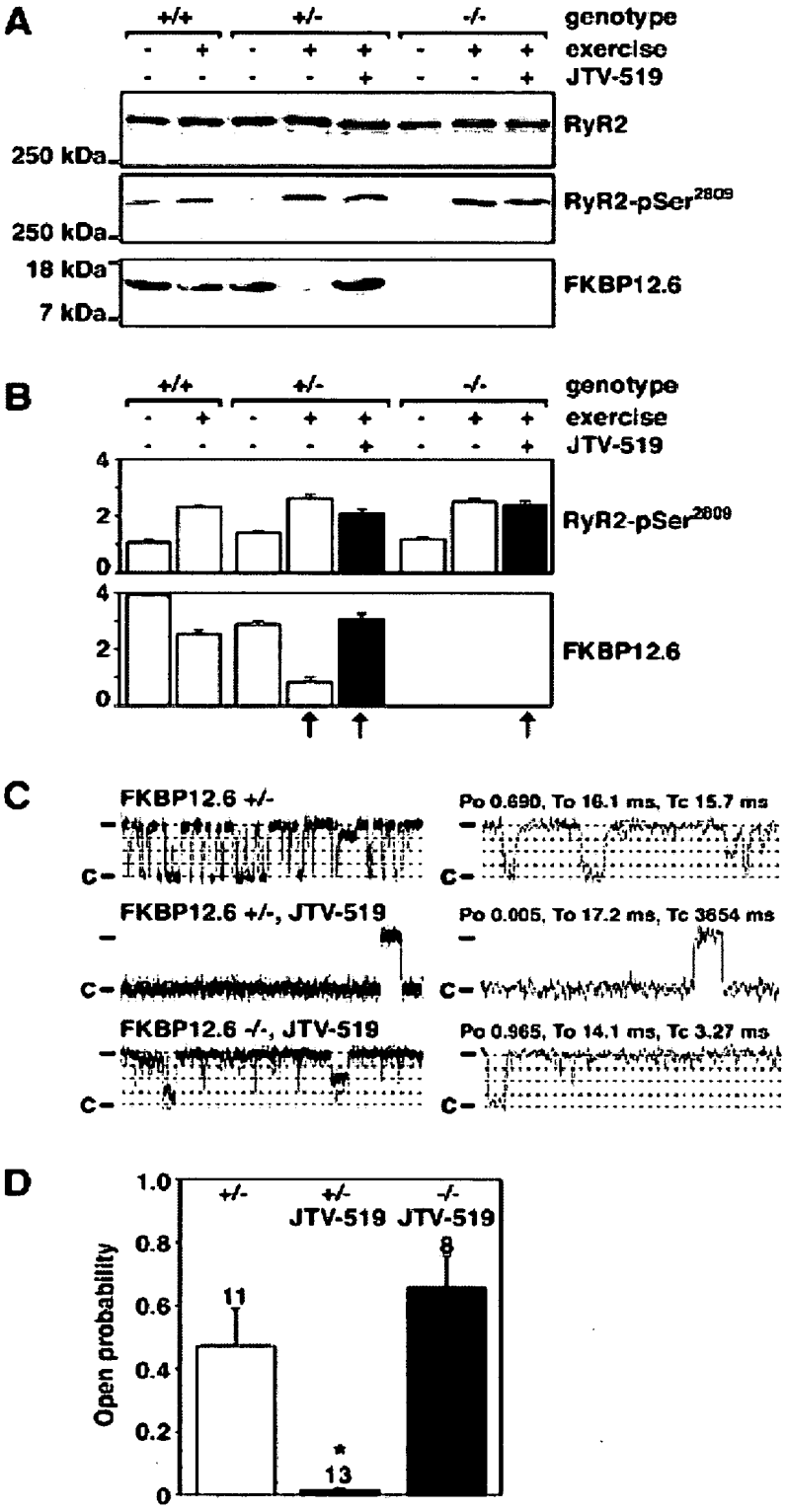
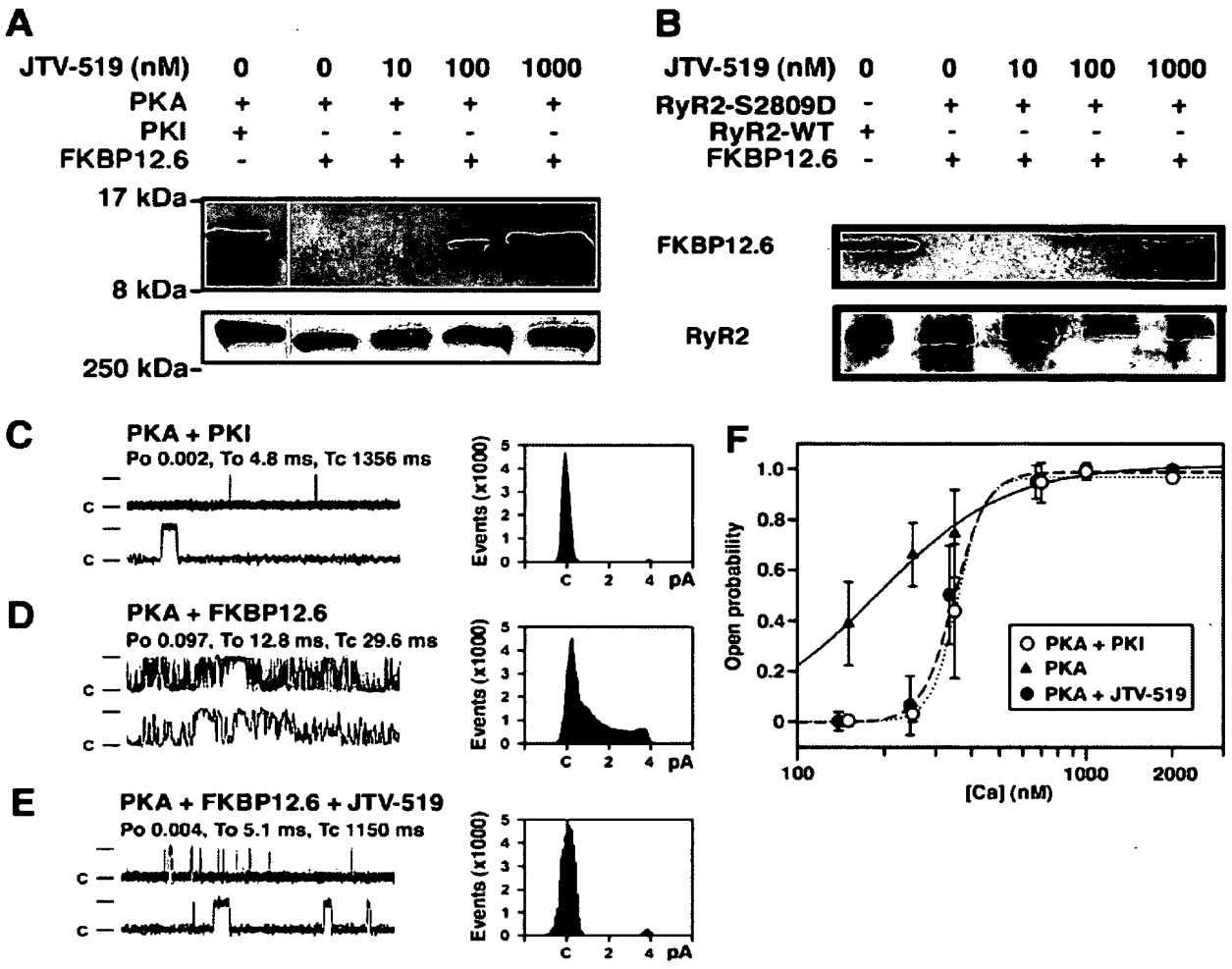

A
+/+
+/-
-/-
genotype
exercise
JTV-519
RyR2
250 kDa
RyR2-pSer2809
250 kDa
18 kDa
7 kDa
FKBP12.6
B
genotype
exercise
JTV-519
RyR2-pSer2809
FKBP12.6
C
FKBP12.6 +/-
Po 0.690, To 16.1 ms, Tc 15.7 ms
FKBP12.6 +/-, JTV-519
Po 0.005, To 17.2 ms, Tc 3654 ms
FKBP12.6 -/-, JTV-519
Po 0.965, To 14.1 ms, Tc 3.27 ms
D
Open probability
JTV-519
JTV-519
11
13
8

Fig. 3/3


A
JTV-519 (nM) 0 0 10 100 1000
PKA + + + + +
PKI + - - - -
FKBP12.6 - + + + +
17 kDa
8 kDa
250 kDa
B
JTV-519 (nM) 0 0 10 100 1000
RyR2-S2809D - + + + +
RyR2-WT + - - - -
FKBP12.6 - + + + +
FKBP12.6
RyR2
C
PKA + PKI
Po 0.002, To 4.8 ms, Tc 1356 ms
D
PKA + FKBP12.6
Po 0.097, To 12.8 ms, Tc 29.6 ms
E
PKA + FKBP12.6 + JTV-519
Po 0.004, To 5.1 ms, Tc 1150 ms
Events (x1000)
c 2 4 pA
F
Open probability
[Ca] (nM)
PKA + PKI
PKA
PKA + JTV-519